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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/736,545	12/17/2003	Masahiro Kawaguchi	03500.017338	6817

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EXAMINER	
LIU, SUE XU	
ART UNIT	PAPER NUMBER
1639	
MAIL DATE	DELIVERY MODE
05/03/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/736,545	KAWAGUCHI ET AL.	
	Examiner	Art Unit	
	Sue Liu	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,6,7 and 27-29* is/are pending in the application.

4a) Of the above claim(s) *27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,6,7,28 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

JON EPPERSON
PRIMARY EXAMINER

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/27/07 has been entered.

Claim Status

2. Claims 1, 3-5, and 8-26 have been canceled as filed on 2/27/07.

Claims 28 and 29 have been added as filed on 2/27/07.

Claims 2, 6, 7, and 27-29 are currently pending;

Claim 27 has been withdrawn.

Claims 2, 6, 7, 28 and 29 are being examined in this application.

Election/Restrictions

3. Applicant's election of Group II (Claims 2-7) in the reply entered on 11/14/2005 was previously acknowledged. Claim 27 has been withdrawn as discussed in the previous office action.

4. Applicants also elected the following species as previously acknowledged:

A.) fluorescent markers;

B.) two kinds of external standard probes;

C.) one kind of internal standard probes;

D.) single-stranded DNA;

E.) 20 residues each of internal and external probes;

F.) two sets of primers that will produce 500 bp and 200 bp products;

G.) a "microorganism"' is selected as the most specific species explicitly recited in the specification;

H.) one nucleic acid;

I.) two.

Priority

5. This application appears to be a CONTINUATION of PCT/JP03/07918 filed on 6/23/03.

Receipt is acknowledged of the following papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file:

A.) An application filed in JAPAN (2002-191390) on 6/28/2002.

B.) An application filed in JAPAN (2002-183249) on 6/24/2002.

Claim Rejections Maintained

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(Note: the instant claim numbers are in bold font.)

Dudley et al

7. Claims 1, 6, 7, 28 and 29 are rejected under 35 U.S.C. **102(b)** as being anticipated by Dudley et al (PNAS. Vol. 99: 7554-7559. May 28, 2002 (cited previously) and the accompanying "Supplementary Material" downloaded from //arep.med.Harvard.edu/masliner/supplement.htm).

The instant claims briefly recite "a DNA micro-array for detecting nucleic acid molecules having target base sequences in a samples, said array comprising:

a substrate; and

nucleic acid probes including base sequences complementary to the target base sequences,

wherein the array contains at least two probes for external standard nucleic acids, said at least two probes having different sequences from each other and having sequences complementary to the external standard nucleic acids,

wherein said at least two probes are available for producing calibration curves for detecting an amount of the nucleic acid molecules having the target base sequences in the sample, and

wherein said at least two probes are provided in different positions on said substrate as spots by use of an ink-jet method."

The specification of the instant application discloses the internal standard probe as "a probe for detecting an internal standard nucleic acid to be used to assist quantitative

determination of a target nucleic acid," and the internal standard nucleic acid as "a nucleic acid of a known base sequence" (page 12 of the specification). The external standard nucleic is also disclosed as "a nucleic acid having a known base sequence to be added to a sample..." and "has no base sequence homology to the base sequence of the target nucleic acid." Therefore, the internal and the external standards and probes could be any nucleic acid sequences that are known, and are not complementary to the target sequences.

Dudley et al, throughout the publication, teach measuring absolute expression with microarrays with a calibrated reference sample, and generating ratios between sample intensities and intensities of the oligo reference measure sample RNA levels (See Abstract of the reference). The reference teaches microarrays comprising probes generated from yeast ORF PCR product set, and an oligo reference sample with certain nucleic acid sequence (See page 7554, right column, 4th paragraph of the reference). The yeast ORF PCR product set contains over 6,000 yeast ORF (see the "Supplementary Material" (p. 9 of Supp.) described on p. 7555, left column, last paragraph of the reference), which could contain the "target nucleic acid" (could be any yeast gene of interest from the >6,000 ORF PCR products). The oligo reference sample could be either the "internal" or "external" probes for the internal or external standards since the oligo sequence is known and contained on the microarray. In addition, any other probes for the >6,000 genes that is not the considered to be the gene of interest (the target gene) and is not complementary to the target gene sequence could be considered as either the internal or the external probes. For example, the RPL29, or the PHO88 genes listed in Figure 3 on Page 7557. The probes for these genes on the microarray would hybridize to genes with different PCR

products (different lengths). The reference further teaches that the microarray are generated either by printing PCR generated cDNA or commercially available oligo sets (See Supplemental Web Site as described on Page 7555, left column, last paragraph of the reference), which would refer to synthetic nucleic acids immobilized on the substrate, and different sequences placed at different positions of **clm 2** because each of the probes is printed at a different spot (see the Supplementary Figure 4). In addition, the reference teaches the oligo reference sample is 20 bases long (page 7554, right column, 4th paragraph of the reference), which would refer to nucleic acid has a chain length of 15 to 75 bases, as recited in **clm 7**. The reference further teaches the Yeast Genome Oligo Set were printed at a concentration of 10 pmols/ml in 150 mM potassium phosphate (See Supplemental Web Site as described on Page 7555, left column, last paragraph of the reference), which reads on probes with the same concentration of **clm 29**. The reference also teaches teaches that the microarray are generated either by printing PCR generated cDNA or commercially available oligo sets (See Supplemental Web Site as described on p. 7555, left column, last paragraph of the reference), which reads on the synthetic nucleic acids immobilized on the substrate as recited in **clm 6**. The reference also teaches resuspending the various PCR products in 150 mM potassium phosphate (Supplemental Material, p. 9), which reads on "spots having different concentrations" of **clm 28**.

The reference also teaches using "OmniGridTM microarrayer" and a piezoelectric printer to print the microarray (Supplemental Material, p. 9, para 1-2), which reads on the recitation of using "ink-jet method" of **clm 1**.

Discussion and Answer to Argument

8. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue the reference does not teach "at least two probes for external standard nucleic acids are provided in different positions on said substrate as spots by use of an ink-jet method". (Reply, p. 5, para 3).

Applicants are respectively directed to the above rejection for detailed discussion on how the cited reference teach each and every element of the instant claimed invention.

Delenstarr et al

9. Claims 2, 6, 7, 28 and 29 are rejected under 35 U.S.C. **102(b)** as being anticipated by Delenstarr et al (US PGPUB 2002/0051973 A1; May 2, 2002; cited previously).

Delenstarr et al, throughout the publication, teach a set of features comprising oligophophodiester probes (reads on microarrays of **clm 2**; Claim 1 of the reference). The reference teaches hybridization features comprising hybridization probes (bound to a surface; Claim 2 of the reference) that selectively hybridize to a detectably labeled target nucleotide sequence (reads on the probes for the target nucleic acid of **clm 2**; Claim 1 of the reference). The reference also teaches background features comprising background probes (as listed in Claim 4 of the reference) that do not selectively hybridize to said nucleotide sequence (read on the internal and/or external probes of **clm 2**; Claims 2 and 4 of the reference). In addition, the reference teaches the features (or array) comprising target probes, test-background probes (read

on either internal or external probes of **clm 2**), and standard-background probes (read on either internal or external probes of **clm 2**); (See Claim 30 of the reference). The reference also teaches the probes could be 25 bases long (such as SEQ ID NO 5 as recited in Claim 5, for example), which reads on the length recited in **clm 7**. Furthermore, the reference recites various different probes with different sequences (such as the one directed in Claim 5 of the reference), which have the functions of hybridizing to PCR products with different chain lengths. The reference further teaches that the probes can be synthesized (See paragraph [0104] of the reference), which reads on limitation of **clm 6**. The reference also teaches using inkjet to print the probes (p. 12, [0126]), which reads on the inkjet printing of **clm 1**. The reference also teaches printing the probes on different spots (e.g. Figure 3), which reads on the different positions of **clm 2**. The reference also teaches the concentration of different probes on the microarray (e.g. Example 6, p. 15+; especially p.11), which reads on the spots having the same or different concentrations of **clms 28 and 29**.

Discussion and Answer to Argument

10. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue the reference does not teach "at least two probes for external standard nucleic acids are provided in different positions on said substrate as spots by use of an ink-jet method". (Reply, p. 5, para 3).

Applicants are respectively directed to the above rejection for detailed discussion on how the cited reference teach each and every element of the instant claimed invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JON EPPERSON
PRIMARY EXAMINER

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Art Unit 1639
4/20/07